
SATB1 reprogrammes gene expression to promote breast tumour growth and metastasis.

Journal: Nature

Publication Year: 2008

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PubMed link: 18337816

Funding Grants: Human Stem Cell Training at UC Berkeley and Childrens Hospital of Oakland

Public Summary:

Scientific Abstract:

Mechanisms underlying global changes in gene expression during tumour progression are poorly understood. SATB1 is a genome organizer that tethers multiple genomic loci and recruits chromatin-remodelling enzymes to regulate chromatin structure and gene expression. Here we show that SATB1 is expressed by aggressive breast cancer cells and its expression level has high prognostic significance ($P < 0.0001$), independent of lymph-node status. RNA-interference-mediated knockdown of SATB1 in highly aggressive (MDA-MB-231) cancer cells altered the expression of >1,000 genes, reversing tumorigenesis by restoring breast-like acinar polarity and inhibiting tumour growth and metastasis in vivo. Conversely, ectopic SATB1 expression in non-aggressive (SKBR3) cells led to gene expression patterns consistent with aggressive-tumour phenotypes, acquiring metastatic activity in vivo. SATB1 delineates specific epigenetic modifications at target gene loci, directly upregulating metastasis-associated genes while downregulating tumour-suppressor genes. SATB1 reprogrammes chromatin organization and the transcription profiles of breast tumours to promote growth and metastasis; this is a new mechanism of tumour progression.

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